Applicant: Hamann et al. Serial No.: 10/712,456

Filed: November 13, 2003

Amendments to the Claims:

Please amend claims 1, 4, 5, 10 and 15 as follows. This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A compound of the formula I

$$R_{2}$$
 R_{3}
 R_{2}
 N
 X
 X

or a pharmaceutically acceptable salt thereof, wherein:

- R₁ is selected from the group consisting of alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and CH₂OR₄;
- R₂ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and CH₂OR₄;
- R₃ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, CH₂OR₄, OR₂, SR₂, halo, NHR₂, NHCOR₄, and NHCONR₄R₄';
- R₄ and R₄' for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;
 - G is selected from the group of among:

Applicant: Hamann *et al*. Serial No.: 10/712,456

Filed: November 13, 2003

wherein:

R₈ is CN;

R₉, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen (H), NO₂, CN, CF₃, OR₄, CO₂R₄, NR₄R₄', CONR₄R₄', CH₂OR₄, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and CR_I;

J, K, L, P, and Q each independently is selected from among NR_{12} , O, S, SO, SO₂ or $CR_{12}R_{12}$ ';

 R_{12} and R_{12} ' in each functional group are each independently selected from a bond or R_1 ;

m is an integer of 0 or 1;

X is a linking group selected from the group consisting of NR₄ and CHR₄;

Y is selected from the group consisting of O, NR₄, NOR₄, S and CH₂; and

Z is -O- or NR_4 ;

with the following provisos:

- (a) when Y is NOR₄, R₄ is not hydrogen;
- (b) when R_1 is methyl,

X is NH, and

Y is O or S, then

Z is not O;

- (c) when (i) R_1 is methyl,
 - (ii) X is NH,
 - (iii) Y is NR₄,
 - (iv) R₄ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and
 - (v) G has the following structure:

Applicant: Hamann et al. Serial No.: 10/712,456

Filed: November 13, 2003

wherein:

R₁₃ is selected from the group consisting of hydrogen, cyano

(-CN), nitro (-NO₂), halo, heterocyclo, OR₁₄, CO₂R₁₅,

 $CONHR_{15}, COR_{15}, S(O)_pR_{15}, \frac{SO_2NR_{15}NR_{15}!}{}$

SO₂NR₁₅R₁₅', NHCOR₁₅ and NHSO₂R₁₅;

R₁₄ in each functional group is independently selected from

the group consisting of hydrogen, alkyl or substituted

alkyl, CHF₂, CF₃ and COR₁₅;

 R_{15} and R_{15} ' in each functional group are each independently selected

from the group consisting of hydrogen, alkyl or

substituted alkyl, alkenyl or substituted alkenyl, alkynyl or

substituted alkynyl, cycloalkyl or substituted cycloalkyl,

heterocycloalkyl or substituted heterocycloalkyl, arylalkyl

or substituted arylalkyl, aryl or substituted aryl, heteroaryl

or substituted heteroaryl and -CN;

AA and BB each independently is selected from the group consisting

of hydrogen, halo, cyano (-CN), nitro (-NO₂), alkyl or

substituted alkyl and OR₁₄; and

p is an integer from 0 to 2,

then Z is not O.

2. and 3. (Cancelled).

4. (Currently amended) The compound of claim 1, or a pharmaceutically acceptable salt of claim 1 thereof, wherein:

 R_1 is alkyl;

R₂ is hydrogen or alkyl;

R₃ is hydroxyl;

X is NR₄;

Y is O; and

Z is O.

Applicant: Hamann *et al.*Serial No.: 10/712,456

Attorney Docket No. 3800024.00560 / 4207 **Amendment Pursuant to 37 C.F.R. §1.312**

Filed: November 13, 2003

5. (Previously presented) A pharmaceutical composition, comprising: a compound or salt of claim 1; and a pharmaceutically acceptable carrier therefor.

- 6. (Previously presented) The pharmaceutical composition of claim 5, further comprising a growth promoting agent.
- 7. (Currently amended) A pharmaceutical composition, comprising:
 a compound of claim 1, or a pharmaceutically acceptable salt thereof, of claim 1; and
 at least one additional therapeutic agent selected from the group consisting of
 parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective
 estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone
 receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents,
 anti-depressants, anti-obesity agents, cardiac glycosides, cholesterol lowering agents,
 anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.
- 8. (Currently amended) A method for treating prostate cancer, comprising: administering to a mammalian species in need of treatment an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereofof claim 1.
 - 9 (Cancelled).
- 10. (Currently amended) A compound selected from the group consisting of 1-(4-Cyano-2-ethyl-3-(trifluoromethyl)phenyl-1-carbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid or a pharmaceutically acceptable salt thereof;
- 1-(4-Cyanonaphthalen-1-ylcarbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;
- 1-(5-Chloro-6-cyano-pyridin-3-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof; and
- 1-[2-(4-Cyanonaphthalen-1-yl)acetyl]-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof.
 - 11. (Previously presented) A pharmaceutical composition, comprising: a compound of claim 10, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier therefor.
- 12. (Previously presented) The pharmaceutical composition of claim 11, further comprising a growth promoting agent.

Filed: November 13, 2003

Applicant: Hamann et al.

Serial No.: 10/712,456

13. (Previously presented) A pharmaceutical composition, comprising:
a compound of claim 10, or a pharmaceutically acceptable salt thereof; and
at least one additional therapeutic agent selected from the group consisting of
parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective
estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone
receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents,
anti-obesity agents, cardiac glycosides, cholesterol lowering agents,
anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

- 14. (Previously presented) A method for treating prostate cancer, comprising: administering to a mammalian species in need of treatment an effective amount of a compound of claim 10 or a pharmaceutically acceptable salt thereof.
 - 15. (Currently amended) A compound of formula I

$$R_{2}$$
 R_{2}
 N
 X
 X

or a pharmaceutically acceptable salt thereof, wherein:

- R₁ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and CH₂OR₄;
- R₂ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and CH₂OR₄;
- R₃ is selected from the group consisting of alkyl or substituted alkyl, and CH₂OR₄;
- R₄ and R₄' for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or

Applicant: Hamann *et al.* Serial No.: 10/712,456

Filed: November 13, 2003

substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;

G is selected from the group consisting of:

$$R_9$$
 R_8
 R_8
 R_8
 R_8
 R_8
 R_8
 R_{10}
 R_{11}
 R_{11}

wherein:

R₈ is CN;

R₉, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen (H), NO₂, CN, CF₃, OR₄, CO₂R₄, NR₄R₄', CONR₄R₄', CH₂OR₄, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F each independently is selected from among N and CR₁;

J, K, L, P, and Q each independently is selected from among NR_{12} , O, S, SO, SO₂ or $CR_{12}R_{12}$ ';

 R_{12} and $R_{12}{}^{\prime}$ in each functional group are each independently selected from a bond or $R_1{}^{\prime}{}_{1}$;

m is an integer of 0 or 1;

X is a linking group selected from the group consisting of NR₄ and CHR₄;

Y is selected from the group consisting of O, NR₄, NOR₄, S and CH₂; and

Z is -O- or NR_4 ;

with the following provisos:

- (a) when Y is NOR₄, R₄ is not hydrogen;
- (b) when R_1 is methyl, X is NH, and Y is O or S, then Z is not O;
- (c) when
 - (i) R_1 is methyl,
 - (ii) X is NH,
 - (iii) Y is NR₄,

Applicant: Hamann et al. Serial No.: 10/712,456

Filed: November 13, 2003

(iv) R₄ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:

wherein:

R₁₃ is selected from the group consisting of hydrogen, cyano

(-CN), nitro (-NO₂), halo, heterocyclo, OR₁₄, CO₂R₁₅,

 $CONHR_{15}, COR_{15}, S(O)_pR_{15}, SO_2NR_{15}NR_{15}$

SO₂NR₁₅R₁₅', NHCOR₁₅ and NHSO₂R₁₅;

 R_{14} in each functional group is independently is selected from

the group consisting of hydrogen, alkyl or substituted

alkyl, CHF₂, CF₃ and COR₁₅;

R₁₅ and R₁₅' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or

substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl,

substituted alkyllyt, cycloarkyt of substituted cycloarkyt,

heterocycloalkyl or substituted heterocycloalkyl, arylalkyl

or substituted arylalkyl, aryl or substituted aryl, heteroaryl

or substituted heteroaryl and CN;

AA and BB each independently is selected from the group consisting

of hydrogen, halo, cyano (-CN), nitro (-NO₂), alkyl or

substituted alkyl and OR_{14} ; and

p is an integer from 0 to 2,

then Z is not O.

16. (Currently amended) A pharmaceutical composition, comprising: a compound of claim 15, or a pharmaceutically acceptable salt thereof of claim 15; and a pharmaceutically acceptable carrier therefor.

Applicant: Hamann *et al.*Serial No.: 10/712,456

Attorney Docket No. 3800024.00560 / 4207 **Amendment Pursuant to 37 C.F.R. §1.312**

Filed: November 13, 2003

17. (Previously presented) The pharmaceutical composition of claim 16, further comprising a growth promoting agent.

- 18. (Currently amended) A pharmaceutical composition, comprising:
 a compound of claim 15, or a pharmaceutically acceptable salt thereof of claim 15; and
 at least one additional therapeutic agent selected from the group consisting of
 parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective
 estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone
 receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents,
 antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents,
 anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.
- 19. (Currently amended) A method for treating prostate cancer, comprising: administering to a mammalian species in need of treatment an effective amount of a compound of claim 15 or a pharmaceutically acceptable salt thereof of claim 15.